

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	3	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	6	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	7	JAN 22	CA/CAPLUS enhanced with patent applications from India
NEWS	8	JAN 29	PHAR reloaded with new search and display fields
NEWS	9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	13	FEB 26	MEDLINE reloaded with enhancements
NEWS	14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	19	MAR 16	CASREACT coverage extended
NEWS	20	MAR 20	MARPAT now updated daily
NEWS	21	MAR 22	LWPI reloaded
NEWS	22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	26	APR 30	CA/CAPLUS enhanced with 1870-1889 U.S. patent records
NEWS	27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	28	MAY 01	New CAS web site launched
NEWS	29	MAY 08	CA/CAPLUS Indian patent publication number format defined
NEWS	30	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS	31	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	32	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	33	MAY 21	CA/CAPLUS enhanced with additional kind codes for German patents
NEWS	34	MAY 22	CA/CAPLUS enhanced with IPC reclassification in Japanese patents
NEWS EXPRESS			NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that

specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 11:08:40 ON 07 JUN 2007

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'CAPLUS' ENTERED AT 11:08:49 ON 07 JUN 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Jun 2007 VOL 146 ISS 24

FILE LAST UPDATED: 6 Jun 2007 (20070606/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s CCR5 receptro?

4761 CCR5

9 RECEPTRO?

L1 0 CCR5 RECEPTRO?

(CCR5(W)RECEPTRO?)

=> s CCR5 receptor?

4761 CCR5

837103 RECEPTOR?

L2 588 CCR5 RECEPTOR?

(CCR5(W)RECEPTOR?)

=> s l2 and mediat?

657942 MEDIAT?

L3 155 L2 AND MEDIAT?

=> s l3 and arthritis?

46462 ARTHRITIS?

L4 13 L3 AND ARTHRITIS?

=> s l13 and py<2002

L13 NOT FOUND

The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s 14 and py<2002
21897378 PY<2002
L5 5 L4 AND PY<2002

=> d ibib abs hitstr tot

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:661253 CAPLUS

DOCUMENT NUMBER: 135:226886

TITLE: Preparation of N-(spiro[benzofuran-3(2H),4'-piperidin]-5-yl)-1,1'-biphenyl-4-carboxamides for treating a CCR5-mediated diseases

INVENTOR(S): Bondinell, William E.; Ku, Thomas W.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

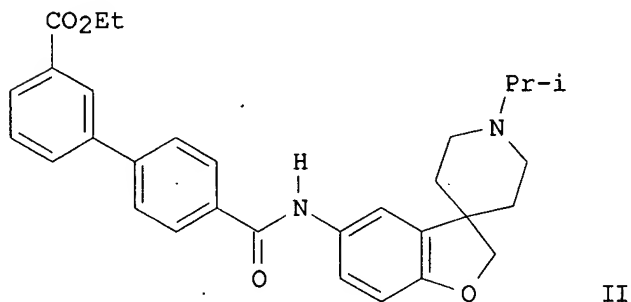
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064213	A1	20010907	WO 2001-US6837	20010302 <--
W:	AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2000-186418P	P 20000302
OTHER SOURCE(S):	MARPAT 135:226886			
GI				



AB The title benzanilides ArAE [I; Ar = (un)substituted biphenyl, Ph; A = CONR, NHCO, CH2NH; R = H, alkyl; E = spiro[benzofuran-3(2H),4'-piperidin]-5-yl, etc.] which are modulators, agonists or antagonists of the CCR5 receptor, were prepared E.g., a multi-step synthesis of the compound II.CF3CO2H, was given. The compds. I showed CCR5 receptor modulator activity having IC50 values in the range of 0.0001-100 μ M. In addition, this invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis, or idiopathic pulmonary fibrosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple

sclerosis, treating and/or preventing rejection of transplanted organs, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic use in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:645845 CAPLUS

DOCUMENT NUMBER: 133:222719

TITLE: Preparation of substituted benzo[1,2-b:5,4-b']dipyrans-4-amines as CCR5 receptor modulators

INVENTOR(S): Blaney, Frank E.; Bondinell, William E.; Chan, James A.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

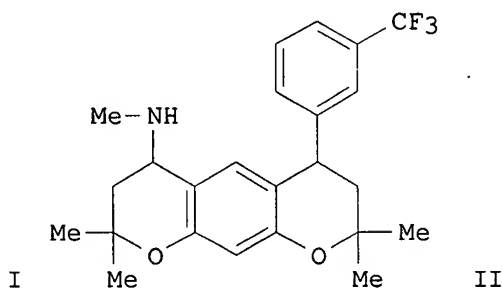
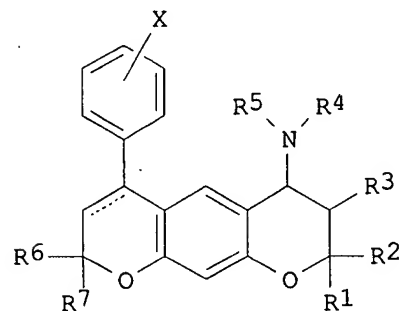
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053175	A1	20000914	WO 2000-US6210	20000310 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156801	A1	20011128	EP 2000-913848	20000310 <--
EP 1156801	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002538203	T	20021112	JP 2000-603664	20000310
AT 270547	T	20040715	AT 2000-913848	20000310
ES 2223481	T3	20050301	ES 2000-913848	20000310
US 6506790	B1	20030114	US 2001-914502	20010829
PRIORITY APPLN. INFO.:			US 1999-123607P	P 19990310
			WO 2000-US6210	W 20000310

OTHER SOURCE(S): MARPAT 133:222719

GI



AB The title compds. (I) [wherein R1, R2, R4, R6, and R7 = independently H or alkyl; R3 = H or OH; R5 = H or (cyclo)alkyl; or NR4R5 = a 5-, 6-, or 7-membered heterocyclic ring; X = H or one or more (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aralkyl, aryl, CH2NR9R10, CH2OR11, COR11, CONR9R10, CO2R11, CN, CF3, NR9R10, NR9COR11, NR9CONR9R10, NO2, OH, alkoxy, acyloxy, etc.; R9 and R10 = independently H, (ar)alkyl, or aryl; or NR9R10 = a 5- or 6-membered heterocyclic ring; R11 = H, (ar)alkyl, aryl, or CF3] were prepared as modulators of the CC chemokine receptor CC-CCR5 (CCR5). Thus, II was synthesized in a 6-step sequence involving (1) cycloaddn. of 3,3-dimethylacrylic acid to resorcinol using H2SO4 to give the 7-hydroxy-2,2-dimethylchromanone, (2) benzyl protection of the hydroxy group, (3) Grignard addition of 3-BrC6H4CF3 to form the chromene, (4) reduction and deprotection using Pd/C, (5) cycloaddn. of 3,3-dimethylacrylic acid using BF3 etherate to give the benzodipyranone, and (6) conversion to the benzodipyranamine with MeNH2 in the presence of TiCl4. I show CCR5 receptor modulator activity with IC50 values ranging from 0.0001 μ M to 100 μ M. I are useful in the treatment and prevention of disease states mediated by CCR5, including asthma and atopic disorders (e.g., atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease. Since CD8+ T cells have been implicated in COPD and CCR5 plays a role in their recruitment, I are also expected to be therapeutic agents for the treatment of COPD. In addition, as modulators of the CCR5 receptor, which is a co-receptor for the entry of HIV into cells, I may be useful in the treatment of HIV infection.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:513446 CAPLUS

DOCUMENT NUMBER: 133:129863

TITLE: Heterocyclic compound modulators of the CCR5 receptor, preparation thereof, and therapeutic use

INVENTOR(S): Bondinell, William E.; Neeb, Michael J.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042852	A1	20000727	WO 2000-US1908	20000125 <--
W:	AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1146790	A1	20011024	EP 2000-909984	20000125 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002535256	T	20021022	JP 2000-594326	20000125
PRIORITY APPLN. INFO.:			US 1999-117044P	P 19990125
			WO 2000-US1908	W 20000125

OTHER SOURCE(S): MARPAT 133:129863

AB Substituted heterocyclic compds. are provided which are modulators, agonists or antagonists of the CCR5 receptor. Also

disclosed is the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted heterocyclic compds. which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:475535 CAPLUS

DOCUMENT NUMBER: 133:99557

TITLE: Substituted benzanilides, their preparation, and their use as CCR5 receptor modulators

INVENTOR(S): Bondinell, William E.; Ku, Thomas W.; Wang, Ning

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040239	A1	20000713	WO 1999-US30888	19991228 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1140072	A1	20011010	EP 1999-967619	19991228 <--
EP 1140072	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002534383	T	20021015	JP 2000-591996	19991228
AT 264100	T	20040415	AT 1999-967619	19991228
ES 2219104	T3	20041116	ES 1999-967619	19991228
PRIORITY APPLN. INFO.:			US 1998-114239P	P 19981230
			US 1999-128010P	P 19990406
			WO 1999-US30888	W 19991228

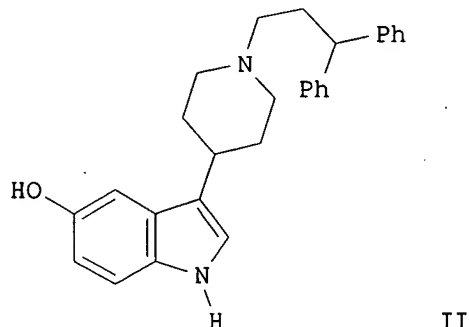
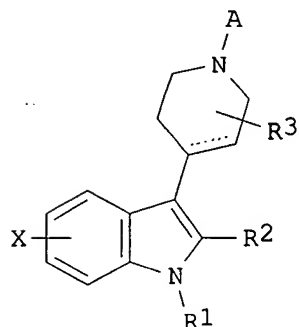
AB Substituted benzanilides are provided which are modulators, agonists or antagonists, of the CCR5 receptor. In addition, the invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:249078 CAPLUS
 DOCUMENT NUMBER: 130:281994
 TITLE: Preparation of 3-(4-piperidinyl or 1,2,3,6-tetrahydro-4-pyridinyl)-1H-indol-5-ols for treating a CCR5-mediated diseases
 INVENTOR(S): Bondinell, William E.; Chan, James; Porter, Roderick A.
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917773	A1	19990415	WO 1998-US21125	19981007 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9809083	A	19990407	ZA 1998-9083	19981006 <--
CA 2305805	A1	19990415	CA 1998-2305805	19981007 <--
AU 9897901	A	19990427	AU 1998-97901	19981007 <--
EP 1037635	A1	20000927	EP 1998-952132	19981007 <--
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001518505	T	20011016	JP 2000-514644	19981007 <--
US 6476028	B1	20021105	US 2000-529338	20000808
PRIORITY APPLN. INFO.:			US 1997-61217P	P 19971007
			WO 1998-US21125	W 19981007
OTHER SOURCE(S):		MARPAT 130:281994		
GI				



AB The title compds. [I; X = H, alkyl, CF₃, etc.; R₁-R₃ = H, alkyl; A = [C(R'')₂]mCR''R₄R₅, [C(R'')₂]nCR''':CR₄R₅; R'' = H, alkyl; m = 0-3; n = 1-2; R₄ = Ph, biphenyl, naphthyl, etc.; R₅ = R'', Ph, naphthyl] which are modulators, agonists or antagonists, of the CCR5 receptor, were prepared E.g., a 3-step synthesis of the title compound II, starting with 5-benzyloxyindole and 1-benzyl-4-piperidone, was given. Compds. I show CCR5 receptor modulator activity having IC₅₀ of 0.0001-100 μM. In addition, this invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis,

sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted 3-(4-piperidinyl)indoles which are CCR5 receptor modulators. Furthermore, since CD8+ T cells have been implicated in Chronic Obstructive Pulmonary Disease ("COPD"), CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of Human Immunodeficiency Virus ("HIV") into cells, receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

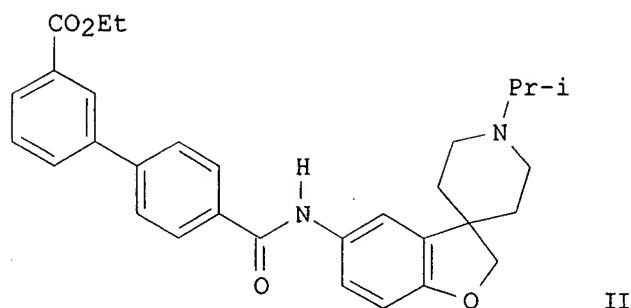
=> s l2 and arthritis?
46462 ARTHRITIS?
L6 29 L2 AND ARTHRITIS?

=> s l6 and py<2002
21897378 PY<2002
L7 8 L6 AND PY<2002

=> d ibib abs hitstr tot

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:661253 CAPLUS
DOCUMENT NUMBER: 135:226886
TITLE: Preparation of N-(spiro[benzofuran-3(2H),4'-piperidin]-5-yl)-1,1'-biphenyl-4-carboxamides for treating a CCR5-mediated diseases
INVENTOR(S): Bondinell, William E.; Ku, Thomas W.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064213	A1	20010907	WO 2001-US6837	20010302 <--
W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-186418P	P 20000302
OTHER SOURCE(S):		MARPAT 135:226886		
GI				



AB The title benzanilides ArAE [I; Ar = (un)substituted biphenyl, Ph; A = CONR, NHCO, CH₂NH; R = H, alkyl; E = spiro[benzofuran-3(2H),4'-piperidin]-5-yl, etc.] which are modulators, agonists or antagonists of the CCR5 receptor, were prepared E.g., a multi-step synthesis of the compound II.CF₃CO₂H, was given. The compds. I showed CCR5 receptor modulator activity having IC₅₀ values in the range of 0.0001-100 μM. In addition, this invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis, or idiopathic pulmonary fibrosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, treating and/or preventing rejection of transplanted organs, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic use in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:435041 CAPLUS

DOCUMENT NUMBER: 135:33431

TITLE: Preparation of cycloamine as CCR5 receptor antagonists

INVENTOR(S): Shiota, Tatsuki; Yokoyama, Tomonori; Kamimura, Takashi

PATENT ASSIGNEE(S): Teijin Limited, Japan

SOURCE: PCT Int. Appl., 271 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

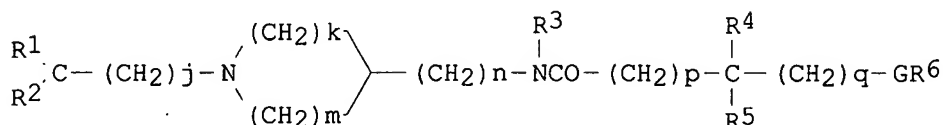
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042208	A1	20010614	WO 2000-JP8627	20001206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393757	A1	20010614	CA 2000-2393757	20001206 <--

AU 200117314	A	20010618	AU 2001-17314	20001206 <--
AU 778173	B2	20041118		
EP 1238970	A1	20020911	EP 2000-979945	20001206
EP 1238970	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 346042	T	20061215	AT 2000-979945	20001206
US 2007010509	A1	20070111	US 2002-148831	20020605
PRIORITY APPLN. INFO.:			JP 1999-348778	A 19991208
			WO 2000-JP8627	W 20001206
OTHER SOURCE(S):		MARPAT 135:33431		
GI				

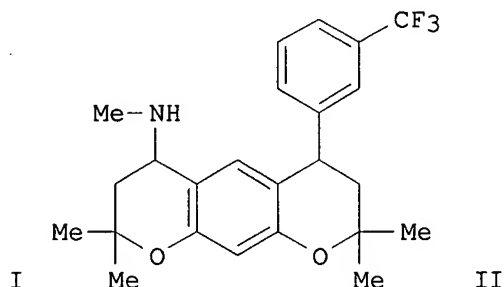
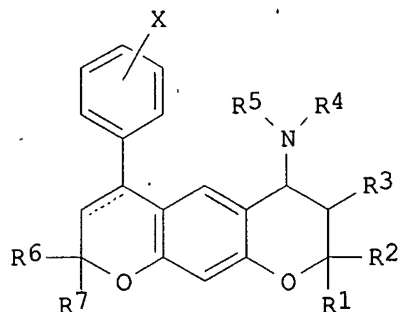


AB Therapeutic or preventive agents for β -chemokine receptor CCR5-related diseases such as AIDS, rheumatoid arthritis, and nephritis, containing as the active ingredient, cyclic amine derivs. such as piperidine and pyrrolidine derivs. of general formula [I; R1 = (un)substituted Ph, C3-8 cycloalkyl, or aromatic heterocyclyl containing 1-3 heteroatoms of O, S, and/N wherein Ph and aromatic heterocyclyl group is optionally condensed to benzene ring or heterocyclyl ring containing 1-3 heteroatoms of O, S, and/N to form an (un)substituted condensed ring; R2 = H, (un)substituted C1-6 alkyl or Ph, C2-7 alkoxy carbonyl, HO; j, k = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted phenyl- optionally substituted C1-6 alkyl; R4, R5 = H, HO, Ph, (un)substituted C1-6 alkyl; or R4 and R5 together represent a 3-6-membered ring cyclic hydrocarbyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NHCONH, NHC(S)NH, NR7SO2, SO2 NR7, NHC(O2, O2CNH (wherein R7 = H, C1-6 alkyl; or R7 and R5 together form C2-5 alkylene); R6 = (un)substituted C3-8 cycloalkyl, C3-6 cycloalkenyl, Ph, benzyl, or aromatic heterocyclyl containing 1-3 heteroatoms of O, S, and/N, wherein Ph, benzyl, and aromatic heterocyclyl are optionally condensed with benzene ring or aromatic heterocyclyl group containing 1-3 heteroatoms of O, S, and/N to form an (un)substituted condensed ring], pharmaceutically acceptable adducts of the same with acids, or pharmaceutically acceptable adducts thereof with C1-6 alkyl, are described. Above CCR5-related diseases include diseases accompanied by destruction of cartilage or bone (in particular chronic rheumatoid arthritis), nephritis or kidney diseases (in particular glomerulonephritis, interstitial nephritis, or nephrosis), demyelinating diseases (in particular multiple sclerosis), post-transplant rejection, host-vs.-graft diseases (GVHD), diabetes, chronic obstructive pulmonary diseases (COPD), bronchial asthma, atopic dermatitis, sarcoidosis, fibrosis, arteriosclerosis, psoriasis, and inflammatory bowel diseases. Thus, 3-(trifluoromethylthio)benzoic acid was condensed with (R)-1-(4-chlorobenzyl)-3-(glycylamino)pyrrolidine using diisopropylcarbodiimide and HOBt in tert-butanol and CHCl3 at room temperature for 15 h to give (R)-1-(4-chlorobenzyl)-3-[[N-(3-(trifluoromethylthio)benzoyl)glycyl]amino]pyrrolidine (II). II and (R)-1-(6-methyl-3-indolylmethyl)-3-[[N-(2-amino-5-(trifluoromethoxy)benzoyl)glycyl]amino]pyrrolidine 10 μ M in vitro inhibited by 20-50% and >80%, resp., the binding of [125I]macrophage inflammatory protein-1 α (MIP-1 α) to CCR5-receptor expressed in CHO cells.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 133:222719
 TITLE: Preparation of substituted benzo[1,2-b:5,4-b']dipyran-4-amines as CCR5 receptor modulators.
 INVENTOR(S): Blaney, Frank E.; Bondinell, William E.; Chan, James A.
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053175	A1	20000914	WO 2000-US6210	20000310 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156801	A1	20011128	EP 2000-913848	20000310 <--
EP 1156801	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002538203	T	20021112	JP 2000-603664	20000310
AT 270547	T	20040715	AT 2000-913848	20000310
ES 2223481	T3	20050301	ES 2000-913848	20000310
US 6506790	B1	20030114	US 2001-914502	20010829
PRIORITY APPLN. INFO.:				
			US 1999-123607P	P 19990310
			WO 2000-US6210	W 20000310
OTHER SOURCE(S):		MARPAT 133:222719		
GI				



AB The title compds. (I) [wherein R1, R2, R4, R6, and R7 = independently H or alkyl; R3 = H or OH; R5 = H or (cyclo)alkyl; or NR4R5 = a 5-, 6-, or 7-membered heterocyclic ring; X = H or one or more (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aralkyl, aryl, CH2NR9R10, CH2OR11, COR11, CONR9R10, CO2R11, CN, CF3, NR9R10, NR9COR11, NR9CONR9R10, NO2, OH, alkoxy, acyloxy, etc.; R9 and R10 = independently H, (ar)alkyl, or aryl; or NR9R10 = a 5- or 6-membered heterocyclic ring; R11 = H, (ar)alkyl, aryl, or CF3] were prepared as modulators of the CC chemokine receptor CC-CCR5 (CCR5). Thus, II was synthesized in a 6-step sequence involving (1) cycloaddn. of 3,3-dimethylacrylic acid to resorcinol using H2SO4 to give the 7-hydroxy-2,2-dimethylchromanone, (2) benzyl protection of the hydroxy group, (3) Grignard addition of 3-BrC6H4CF3 to form the chromene, (4) reduction

and deprotection using Pd/C, (5) cycloaddn. of 3,3-dimethylacrylic acid using BF₃ etherate to give the benzodipyrone, and (6) conversion to the benzodipyrnamine with MeNH₂ in the presence of TiCl₄. I show CCR5 receptor modulator activity with IC₅₀ values ranging from 0.0001 μ M to 100 μ M. I are useful in the treatment and prevention of disease states mediated by CCR5, including asthma and atopic disorders (e.g., atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease. Since CD8+ T cells have been implicated in COPD and CCR5 plays a role in their recruitment, I are also expected to be therapeutic agents for the treatment of COPD. In addition, as modulators of the CCR5 receptor, which is a co-receptor for the entry of HIV into cells, I may be useful in the treatment of HIV infection.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:513446 CAPLUS

DOCUMENT NUMBER: 133:129863

TITLE: Heterocyclic compound modulators of the CCR5 receptor, preparation thereof, and therapeutic use

INVENTOR(S): Bondinell, William E.; Neeb, Michael J.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042852	A1	20000727	WO 2000-US1908	20000125 <--
W:			AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
EP 1146790	A1	20011024	EP 2000-909984	20000125 <--
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO	
JP 2002535256	T	20021022	JP 2000-594326	20000125
PRIORITY APPLN. INFO.:			US 1999-117044P	P 19990125
			WO 2000-US1908	W 20000125

OTHER SOURCE(S): MARPAT 133:129863

AB Substituted heterocyclic compds. are provided which are modulators, agonists or antagonists of the CCR5 receptor. Also disclosed is the treatment and prevention of disease states mediated by CCR5, including, but no limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted heterocyclic compds. which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:475535 CAPLUS
DOCUMENT NUMBER: 133:99557
TITLE: Substituted benzanilides, their preparation, and their use as CCR5 receptor modulators
INVENTOR(S): Bondinell, William E.; Ku, Thomas W.; Wang, Ning
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040239	A1	20000713	WO 1999-US30888	19991228 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1140072	A1	20011010	EP 1999-967619	19991228 <--
EP 1140072	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002534383	T	20021015	JP 2000-591996	19991228
AT 264100	T	20040415	AT 1999-967619	19991228
ES 2219104	T3	20041116	ES 1999-967619	19991228
PRIORITY APPLN. INFO.:			US 1998-114239P	P 19981230
			US 1999-128010P	P 19990406
			WO 1999-US30888	W 19991228

AB Substituted benzanilides are provided which are modulators, agonists or antagonists, of the CCR5 receptor. In addition, the invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

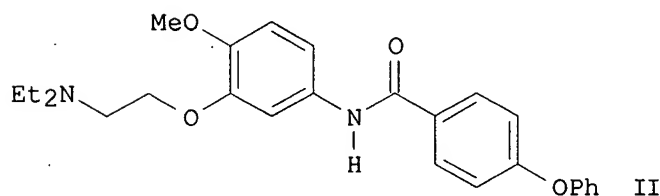
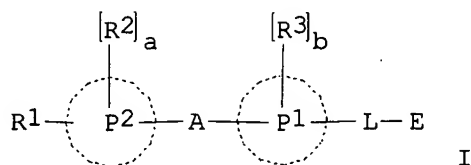
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:98304 CAPLUS
DOCUMENT NUMBER: 132:151564
TITLE: Preparation of substituted anilides as modulators, agonists or antagonists of the CCR5 receptor
INVENTOR(S): Ku, Thomas W.; Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006146	A1	20000210	WO 1999-US17121	19990728 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338764	A1	20000210	CA 1999-2338764	19990728 <--
AU 9952392	A	20000221	AU 1999-52392	19990728 <--
BR 9912406	A	20010424	BR 1999-12406	19990728 <--
EP 1100485	A1	20010523	EP 1999-937589	19990728 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100267	T2	20010921	TR 2001-200100267	19990728 <--
HU 200102752	A2	20011228	HU 2001-2752	19990728 <--
JP 2002521436	T	20020716	JP 2000-562001	19990728
IN 2001MN00076	A	20050304	IN 2001-MN76	20010118
NO 2001000446	A	20010126	NO 2001-446	20010126 <--
PRIORITY APPLN. INFO.:---			US 1998-94406P	P 19980728
			US 1999-134157P	P 19990514
			WO 1999-US17121	W 19990728

OTHER SOURCE(S): MARPAT 132:151564
GI



AB The title compds. [I; the basic N in moiety E may be optionally quaternized with alkyl or is optionally present as the N-oxide; P1, P2 = Ph, fused bicyclic aryl, monocyclic heterocyclyl, etc.; A = CO, O, SOc, etc.; L = CH₂NH, NHCH₂, etc.; R1, R2 = H, alkyl, alkenyl, etc.; R3 = H, alkyl, cycloalkyl, etc.; a, b = 1-3; c = 0-2] which are modulators, agonists or antagonists of the CCR5 receptor, and therefore useful in treating COPD, asthma and atopic disorders, rheumatoid arthritis, atherosclerosis, sarcoidosis and other fibrotic disease, psoriasis, autoimmune diseases such as multiple sclerosis, inflammatory bowel disease, and HIV, were prepared E.g., a synthesis of benzamide II starting with (4-formyl-3,5-dimethoxyphenoxy)-Merrifield resin and 3-[2-(diethylamino)ethoxy]-4-methoxyaniline, was given. Compds. I show CCR5 receptor modulator activity having IC₅₀ values of 0.0001 to 100 μ M.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:461743 CAPLUS
DOCUMENT NUMBER: 131:241862
TITLE: CCR5+ and CXCR3+ T cells are increased in multiple sclerosis and their ligands MIP-1 α and IP-10 are expressed in demyelinating brain lesions
AUTHOR(S): Balashov, Konstantin E.; Rottman, James B.; Weiner, Howard L.; Hancock, Wayne W.
CORPORATE SOURCE: Center for Neurologic Diseases, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(12), 6873-6878
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Multiple sclerosis (MS) is a T cell-dependent chronic inflammatory disease of the central nervous system. The role of chemokines in MS and its different stages is uncertain. Recent data suggest a bias in expression of chemokine receptors by Th1 vs. Th2 cells; human Th1 clones express CXCR3 and CCR5 and Th2 clones express CCR3 and CCR4. Chemokine receptors expressed by Th1 cells may be important in MS, as increased interferon- γ (IFN- γ) precedes clin. attacks, and IFN- γ injection induces disease exacerbations. The authors found CXCR3+ T cells increased in blood of relapsing-remitting MS, and both CCR5+ and CXCR3+ T cells increased in progressive MS compared with controls. Furthermore, peripheral blood CCR5+ T cells secreted high levels of IFN- γ . In the brain, the CCR5 ligand, MIP-1 α , was strongly associated with microglia/macrophages, and the CXCR3 ligand, IP-10, was expressed by astrocytes in MS lesions but not unaffected white matter of control or MS subjects. Areas of plaque formation were infiltrated by CCR5-expressing and, to a lesser extent, CXCR3-expressing cells; interleukin (IL)-18 and IFN- γ were expressed in demyelinating lesions. No leukocyte expression of CCR3, CCR4, or 6 other chemokines, or anti-inflammatory cytokines IL-5, IL-10, IL-13, and transforming growth factor- β was observed. Thus, chemokine receptor expression may be used for immunol. staging of MS and potentially for other chronic autoimmune/inflammatory processes such as rheumatoid arthritis, autoimmune diabetes, or chronic transplant rejection. Furthermore, these results provide a rationale for the use of agents that block CCR5 and/or CXCR3 as a therapeutic approach in the treatment of MS.

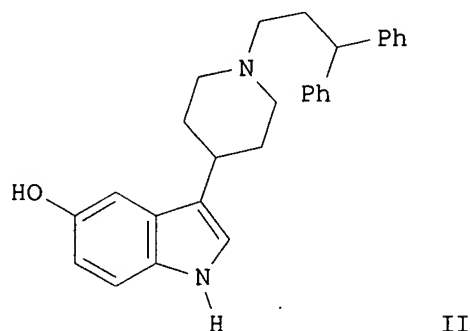
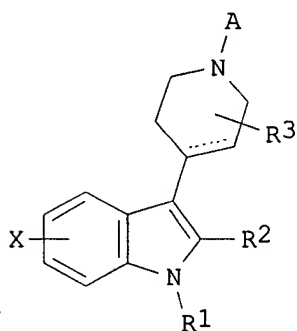
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:249078 CAPLUS
DOCUMENT NUMBER: 130:281994
TITLE: Preparation of 3-(4-piperidinyl or 1,2,3,6-tetrahydro-4-pyridinyl)-1H-indol-5-ols for treating a CCR5-mediated diseases
INVENTOR(S): Bondinell, William E.; Chan, James; Porter, Roderick A.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

WO 9917773	A1	19990415	WO 1998-US21125	19981007 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9809083	A	19990407	ZA 1998-9083	19981006 <--
CA 2305805	A1	19990415	CA 1998-2305805	19981007 <--
AU 9897901	A	19990427	AU 1998-97901	19981007 <--
EP 1037635	A1	20000927	EP 1998-952132	19981007 <--
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001518505	T	20011016	JP 2000-514644	19981007 <--
US 6476028	B1	20021105	US 2000-529338	20000808
PRIORITY APPLN. INFO.:			US 1997-61217P	P 19971007
			WO 1998-US21125	W 19981007
OTHER SOURCE(S):		MARPAT 130:281994		
GI				



AB The title compds. [I; X = H, alkyl, CF₃, etc.; R₁-R₃ = H, alkyl; A = [C(R'')₂]mCR'''R₄R₅, [C(R'')₂]nCR'''CR₄R₅; R'' = H, alkyl; m = 0-3; n = 1-2; R₄ = Ph, biphenyl, naphthyl, etc.; R₅ = R'', Ph, naphthyl] which are modulators, agonists or antagonists, of the CCR5 receptor, were prepared E.g., a 3-step synthesis of the title compound II, starting with 5-benzoyloxyindole and 1-benzyl-4-piperidone, was given. Compds. I show CCR5 receptor modulator activity having IC₅₀ of 0.0001-100 μM. In addition, this invention relates to the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted 3-(4-piperidinyl)indoles which are CCR5 receptor modulators. Furthermore, since CD8+ T cells have been implicated in Chronic Obstructive Pulmonary Disease ("COPD"), CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of Human Immunodeficiency Virus ("HIV") into cells, receptor modulators may be useful in the treatment of HIV infection.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE
COST IN U.S. DOLLARS

SINCE FILE TOTAL

FULL ESTIMATED COST	ENTRY 57.23	SESSION 57.44
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.14	-10.14

FILE 'STNGUIDE' ENTERED AT 11:11:48 ON 07 JUN 2007
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Jun 4, 2007 (20070604/UP).

=> d his

(FILE 'HOME' ENTERED AT 11:08:40 ON 07 JUN 2007)

FILE 'CAPLUS' ENTERED AT 11:08:49 ON 07 JUN 2007

L1	0 S CCR5 RECEPTRO?
L2	588 S CCR5 RECEPTOR?
L3	155 S L2 AND MEDIAT?
L4	13 S L3 AND ARTHRITIS?
L5	5 S L4 AND PY<2002
L6	29 S L2 AND ARTHRITIS?
L7	8 S L6 AND PY<2002

FILE 'STNGUIDE' ENTERED AT 11:11:48 ON 07 JUN 2007

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.18	57.62
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-10.14

STN INTERNATIONAL LOGOFF AT 11:13:39 ON 07 JUN 2007